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CAPUTA, A EXAMINER

18N1/1130

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ART UNIT	PAPER NUMBER
1806	11

DATE MAILED: 11/30/95

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 9/5/95 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 1-121 are pending in the application.
   Of the above, claims 13-39, 41-60, and 62-121 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1-12, 40, and 61 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

Part III DETAILED ACTION

Election/Restriction

1. Applicant's election of Group I, claims 1-12 and 61 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (M.P.E.P. § 818.03(a)). Upon further consideration by the Examiner the election of species is withdrawn.

2. Newly amended claims 1, 6, 12, and 40 are directed to the nucleic acid and host cells of Group I and IX as set forth in the original restriction (see Paper No. 8). Since Group I drawn to the nucleic acid comprising *Cry j* I and Group IX drawn to the nucleic acid coding for *Cry j* II are distinct for the reasons set forth in Paper No. 8, said claims will be examined to the extent said claims read on Cry j I.

3. Claims 13-39, 41-60, and 62-121 are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention was made **without** traverse in Paper No. 10.

Claim Rejections - 35 USC § 112

4. Claims 1-12, 40, and 61 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 6, and 12 are rejected since it is not clear what the metes of the claimed subject matter. Do applicants intend the claimed subject matter to encompass a chromosome?

Claim 5 is rejected for use of the term "consists essentially" since said term is not used to define the metes and bounds of a claimed compound.

Claim 61 is rejected since it refers to a claim which was withdrawn from consideration.

5. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to adequately teach one of ordinary skill in the art how to make and use the claimed invention, i.e. failing to provide an enabling disclosure.

a. The specification provides insufficient guidance to a nucleic acid coding for the Cry I j species as broadly claimed which encompass modifications (i.e. deletions, additions, functional equivalents, or fragments). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of deletions, additions, or modifications broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative species. The amino acid sequence of a protein determines its structural and functional properties, and the predictability of which changes can be tolerated in a protein's amino acid sequence and still retain similar activity/utility requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. While recombinant and mutagenesis techniques are known, it is **not** routine in the

art to screen for positions within the protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining similar activity/utility are limited in any protein and the result of such modifications is unpredictable based on the instant disclosure. One skilled in the art would expect any tolerance to modification shown for a given protein to diminish with each further and additional modification, e.g. multiple deletions. The sequence of some proteins is highly conserved and one skilled in the art would not expect tolerance to any amino acids modification in such proteins. Bowie et al. (Science 247:1306-1310) teach positions in the sequence that are critical to the protein's structure/function relationship, can tolerate only relatively conservative substitutions or no substitutions (see pages 1306-1310, especially p. 1306, column 2). Furthermore Kumar et al. (PNAS 87:1337-1341 1990) teach amino acid variations at a single residue of a peptide can affect T cell activation and other properties. The specification does not support the broad scope of the claims because the specification does **not** disclose the specific positions which can be predictably modified and which regions are critical.

Thus, applicants have **not** provided sufficient guidance to enable one skilled in the art to make and use the claimed protein in manner reasonably correlated with the scope of the claims broadly including any number of deletions of any size. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made in the proteins structure and still maintain activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991) at 18 USPQ2d 1026-1027, Ex parte

Forman, 230 U.S.P.Q. 546 (Bd. Pat. App. & Int. 1986), and Ex parte Anderson, 30 USPQ 2d 1866 (Bd. Pat. App. & Int. 1993).

b. The specification describes the nucleic acid sequence coding for *Cry j* I and the deduced amino acid sequence (page 7). The specification teaches the purification and cloning of Cry j I. The specification also discloses peptides of Cry j I that have T cell stimulating activity. The specification disclose binding assays of IgE to purified and recombinant Cry j I and histamine release analysis. The specification does not identify particular antigenic fragments that modify B cell responses. The specification does not identify particular antigenic fragments that bind IgE but do not result in mediator release. The specification also does not identify which modifications to *Cry j* I would result in the reduction of an allergic response following the administration of the modified *Cry j* I. The specification also does not identify fragments or proteins of the peptides having T cell epitopes of *Cry j* I or any of the other properties listed above. In the absence of evidence to the contrary, it would require undue experimentation to test the isolate the nucleic acid encoding the *Cry j* I fragments, functional equivalents, or peptides for the properties listed above.

6. Claims 1-12, 40, and 61 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Anthony C. Caputa, whose telephone number is (703)-308-3995. The examiner can be reached on Monday-Thursday from 8:30 AM-6:00 PM.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703)-308-0196.

Papers related to this application may be submitted to Art Unit 1806 by facsimile transmission. The faxing of such papers must conform with the notice published in the official Gazette 1096 OG 30 (November 15, 1989). The Fax number is (703)-305-3014.

Anthony C. Caputa, Ph.D.
November 25, 1995

ANTHONY C. CAPUTA
PATENT EXAMINER
GROUP 1800